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     (FILE 'HOME' ENTERED AT 08:20:59 ON 25 OCT 2006)

     FILE 'REGISTRY' ENTERED AT 08:22:17 ON 25 OCT 2006
L1                STRUCTURE UPLOADED
L2                QUE L1
L3              1 S L2 SSS SAM
L4            174 S L2 SSS FULL

     FILE 'CAPLUS' ENTERED AT 08:23:19 ON 25 OCT 2006
L5             45 S L4
L6         306153 S CANCER
                  E TUMOR+ALL/CT
L7         434934 S TUMOR
L8         439845 S NEOPLASM
L9          56612 S NEOPLASTIC
L10            10 S L5 AND (L6 OR L7 OR L8 OR L9)
L11            35 S L5 NOT L10
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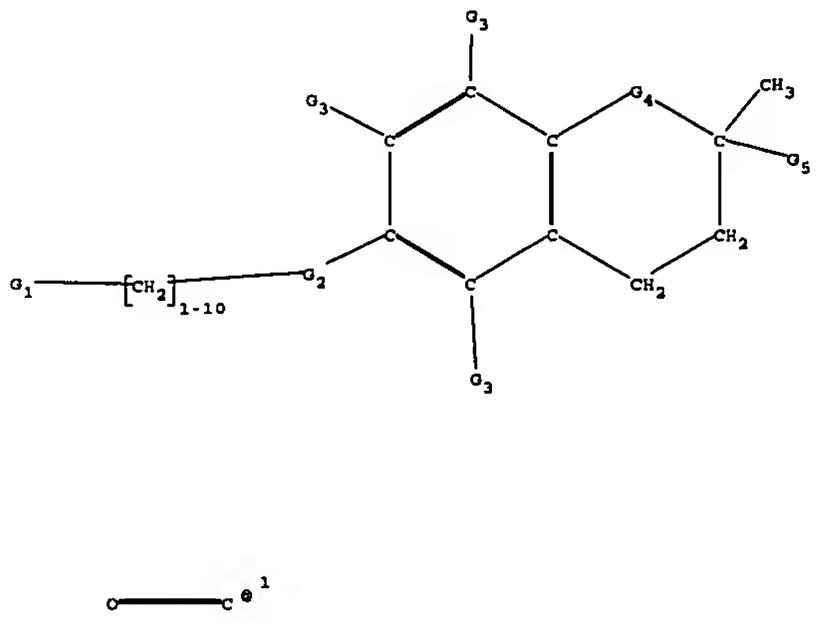
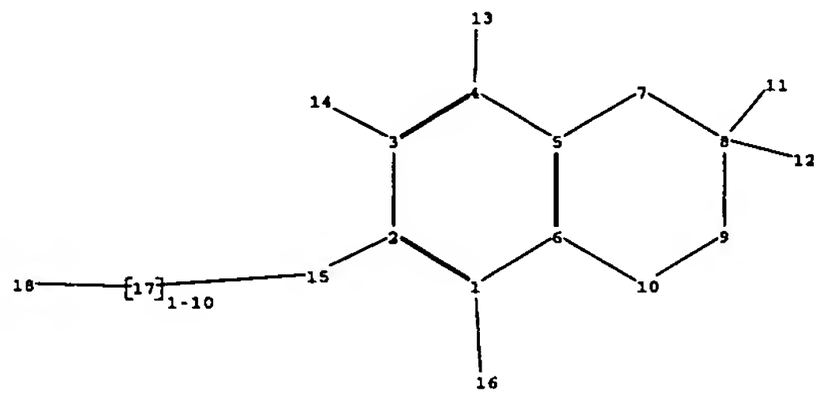
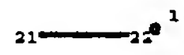
C:\Program Files\Stnexp\Queries\10644418.str







29

chain nodes :
11 12 13 14 15 16 17 18 21 22 29
ring nodes :
1 2 3 4 5 6 7 8 9 10
chain bonds :
1-16 2-15 3-14 4-13 8-11 8-12 15-17 17-18 21-22
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10
exact/norm bonds :
1-16 2-15 3-14 4-13 5-7 6-10 7-8 8-9 8-11 8-12 9-10 15-17 17-18 21-22
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

G1:O,N,[*1]

G2:O,S,N

G3:H,CH3

G4:O,N

G5:COOH,Ak

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:CLASS 12:CLASS
13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 21:CLASS 22:CLASS 29:CLASS

High performance liquid chromatography (HPLC) analyses are conducted on serum and tissue samples at weekly intervals during the 30 day treatment. Compound 1 is detected in the serum and tissues from all three test groups.

EXAMPLE 16

Preparation of Stock Solution, Vehicle and Compound 1 Dilutions

Stock Solution of Compound 1

Dissolve 2 grams of compound #1 in 5 mls of 100% ethanol (ETOH) and vortex at 37° C.

Compound 1 at 20 mg/0.1 ml gavage/mouse:

Combine 1 ml of compound 1 stock solution, 3 mls of vitamin E depleted peanut oil and 400 mg of compound #1 (dry) and vortex at 37° C.

Compound 1 at 10 mg/0.1 ml gavage/mouse:

Combine 1 ml of compound 1 stock solution and 3 mls of vitamin E depleted peanut oil.

Compound 1 at 5 mg/0.1 ml gavage/mouse:

Combine 0.5 ml of compound 1 stock solution and 3 mls of vitamin E depleted peanut oil.

Vehicle:

Combine 1 ml ETOH 3 mls of vitamin E depleted peanut oil.

EXAMPLE 17

Chemopreventive Properties of Compound 1 in an ACI Rat Cancer Model

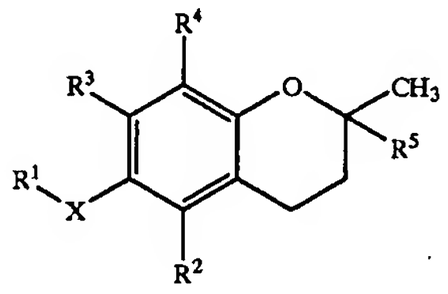
Compound 1 is used in vivo to treat transplanted human breast, prostate, and colon tumors transplanted in immune compromised nude mice. The chemopreventive effectiveness of compound 1 in vivo against human breast cancer is shown in an estrogen cancer initiated ACI rat breast cancer model. Approximately 90% of rats implanted with estrogen pellets develop breast cancer within 6 months after estrogen implantation.

Compound 1 is dissolved in 100% ethanol and is diluted to the appropriate dosage using vitamin E depleted peanut oil. The maximum tolerated dose (MTD, maximum dose of compound that can be administered without adverse affects) is determined as described in Examples 14 and 15. Compound 1 is administered at MTD and ½ MTD. ACI rats at 4 weeks of age are subpannicularly implanted with estrogen pellets in the shoulder region. Compound 1 at MTD and ½ MTD is administered by gavage Breast tumors are detected in the control group at approximately 100 days following estrogen implantation. Ninety percent of the control rats develop breast cancer within 6 months after estrogen implantation. Tumor bearing animals from control and treatment groups are sacrificed at various time intervals after treatment initiation, and mammary tissue is examined for obvious tumors, and further examined by histological analyses.

One skilled in the art will readily appreciate that the present invention is well adapted to carry out the objects and obtain the ends and advantages mentioned, as well as those inherent therein. The present examples along with the methods, procedures, treatments, molecules, and specific compounds described herein are presently representative of preferred embodiments, are exemplary, and are not intended as limitations on the scope of the invention. Changes therein and other uses will occur to those skilled in the art which are encompassed within the spirit of the invention as defined by the scope of the claims.

What is claimed is:

1. A method for the treatment of a cell proliferative disease comprising administering to an animal a pharmacologically effective dose of a compound having a structural formula:



wherein X is oxygen;

R^1 is —C_{1-10} alkylene-COOH —C_{1-4} alkylene-CONH2, —C_{1-4} alkylene-COO—C_{1-4} alkyl, —C_{1-4} alkylene-CON(C_{1-4} alkylene-COOH)$_2$, C_{1-4} alkylene-OH, C_{1-4}alkylene-NH_3-halo, or C_{1-4} alkylene-OSO_2NH (C_{1-4} alkyl)$_3$;

R^2, R^3 are H or C_{1-4} alkyl;

R^4 is C_{1-4} alkyl; and

R^5 is methyl, C_{7-17} alkyl, COOH, C_{7-17} olefinic group containing 3 to 5 ethylenic bonds, —C═C—COO—C_{1-4} alkyl or C_{1-4} alkylene-COO—C_{1-4} alkyl with the proviso that R^1 cannot be —C_{2-4} alkylene-COOH when R^2, R^3, and R^4 are methyl, and R^5 is a C_{16} alkyl; or a pharmaceutical composition thereof.

2. The method of claim 1, wherein said compound is selected from the group consisting of 2,5,7,8-tetramethyl-(2R-(4R,8R, 12-trimethyltridecyl)chroman-6-yloxy) acetic acid, 2,5,8-trimethyl-(2R-(4R,8R,12-trimethyltridecyl) chroman-6-yloxy)acetic acid, 2,7,8-trimethyl-(2R-(4R,8R, 12-trimethyltridecyl) chroman-6-yloxy) acetic acid, 2,8-dimethyl-(2R-(4R,8R,12-trimethyltridecyl)chroman-6-yloxy) acetic acid, 2-(N,N-(carboxymethyl)-2(2,5,7,8-tetramethyl-(2R-(4R,8R,12-trimethyltridecyl) chroman-6-yloxy) acetic acid, 2,5,7,8-tetramethyl-(2RS-(4RS,8RS,12-trimethyltridecyl)chroman-6-yloxy)acetic acid, 2,5,7,8-tetramethyl-2R-(2RS,6RS,10-trimethylundecyl)chroman-6-yloxy) acetic acid, 3-(2,5,7,8-tetramethyl-(2R-(4R,8,12-trimethyltridecyl)chroman-6-yloxy)propyl-1-ammonium chloride, 2,5,7,8-tetramethyl-(2R-(4r,8R,12-trimethyltridecyl)chroman-3-ene-6-yloxy) acetic acid, 2-(2,5,7,8-tetramethyl-(2R-(4R,8,12-trimethyltridecyl) chroman-6-yloxy)triethylammonium sulfate, 6-(2,5,7,8-tetramethyl-(2R(4R,8,12-trimethyltridecyl)chroman)acetic acid, 2,5,7,8,-tetramethyl-(2R-(heptadecyl)chroman)yloxy) acetic acid, and 2,5,7,8,-tetramethyl-2R(4,8,-dimethyl-1,3,7 E:Z nonotrien)chroman-6-yloxy) acetic acid.

3. The method of claim 1, wherein said compound exhibits an anti-proliferative effect comprising apoptosis, DNA synthesis arrest, cell cycle arrest, or cellular differentiation.

4. The method of claim 1, wherein said animal is a human.

5. The method of claim 1, wherein said composition is administered in a dose of from about 1 mg/kg to about 60 mg/kg.

6. The method of claim 1, wherein administration of said composition is selected from the group consisting of oral, topical, intraocular, intranasal, parenteral, intravenous, intramuscular, or subcutaneous.

7. The method of claim 1, wherein said cell proliferative disease is selected from the group consisting of neoplastic diseases and non-neoplastic disorders.

8. The method of claim 7, wherein said neoplastic disease is selected from the group consisting of ovarian cancer,

cervical cancer, endometrial cancer, bladder cancer, lung cancer, breast cancer, testicular cancer, prostate cancer, gliomas, fibrosarcomas, retinoblastomas, melanomas, soft tissue sarcomas, ostersarcomas, leukemias, colon cancer, carcinoma of the kidney, pancreatic cancer, basal cell carcinoma, and squamous cell carcinoma.

9. The method of claim **7**, wherein said non-neoplastic disease is selected from the group consisting of psoriasis, benign proliferative skin diseases, ichthyosis, papilloma, restinosis, scleroderma, hemangioma, viral diseases, and autoimmune diseases.

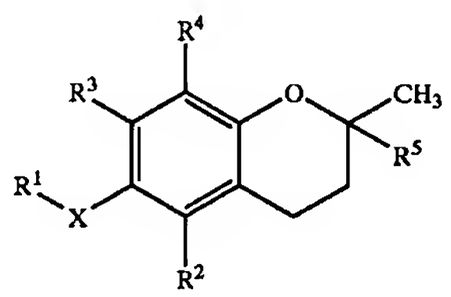
10. The method of claim **9**, wherein said autoimmune diseases are selected from the group consisting of autoimmune thyroiditis, multiple sclerosis, myasthenia gravis, systemic lupus erythematosus, dermatitis herpetiformis, celiac disease, and rheumatoid arthritis.

11. The method of claim **7**, wherein said non-neoplastic disorders are selected from the group consisting of viral disorders and autoimmune disorders.

12. The method of claim **11**, wherein said viral disorder is Human Immunodeficiency Virus.

13. The method of claim **11**, wherein said autoimmune disorders are selected from the group consisting of the inflammatory process involved in cardiovascular plaque formation, ultraviolet radiation induced skin damage and disorders involving an immune component.

14. A method of inducing apoptosis of a cell, comprising the step of contacting said cell with a pharmacologically effective dose of a compound having a structural formula:



wherein X is oxygen;

R^1 is —C_{1-10} alkylene-COOH —C_{1-4} alkylene-CONH2, —C_{1-4} alkylene-COO—C_{1-4} alkyl, —C_{1-4} alkylene-$CON(C_{1-4}$ alkylene-$COOH)_2$, C_{1-4} alkylene-OH, C_{1-4} alkylene-NH_3-halo, or C_{1-4} alkylene-$OSO_2NH(C_{1-4}$ alkyl$)_3$;

R^2, R^3 are H or C_{1-4} alkyl;

R^4 is C_{1-4} alkyl; and

R^5 is methyl, C_{7-17} alkyl, COOH, C_{7-17} olefinic group containing 3 to 5 ethylenic bonds, —C═C—COO—C_{1-4} alkyl or C_{1-4} alkylene-COO—C_{1-4} alkyl with the proviso that R^1 cannot be —C_{2-4} alkylene-COOH when R^2, R^3, and R^4 are methyl, and R^5 is a C_{16} alkyl; or a pharmaceutical composition thereof.

15. The method of claim **14**, wherein said compound is selected from the group consisting of 2,5,7,8-tetramethyl-(2R(4R,8R,12-trimethyltridecyl)chroman-6-yloxy)acetic acid, 2,5,8-trimethyl-(2R-(4R,8R,12-trimethyltridecyl) chroman-6-yloxy)acetic acid, 2,7,8-trimethyl-(2R-(4R,8R, 12-trimethyltridecyl)chroman-6-yloxy)acetic acid, 2,8-dimethyl-(2R-(4R,8R,12-trimethyltridecyl)chroman-6-yloxy) acetic acid, 2-(N,N-(carboxymethyl)-2(2,5,7,8-tetramethyl-(2R-(4R,8R, 12-trimethyltridecyl) chroman-6-yloxy) acetic acid, 2,5,7,8-tetramethyl-(2RS-(4RS,8RS, 12-trimethyltridecyl)chroman-6-yloxy)acetic acid, 2,5,7,8-tetramethyl-2R-(2RS,6RS,10-trimethylundecyl)chroman-6-yloxy)acetic acid, 3-(2,5,7,8-tetramethyl-(2R-(4R,8,12-trimethyltridecyl)chroman-6-yloxy)propyl-1-ammonium chloride, 2,5,7,8-tetramethyl-(2R-(4r,8R,12-trimethyltridecyl)chroman-3-ene-6-yloxy) acetic acid, 2-(2,5,7,8-tetramethyl-(2R-(4R,8,12-trimethyltridecyl) chroman-6-yloxy)triethylammonium sulfate, 6-(2,5,7,8-tetramethyl-(2R-(4R,8,12-trimethyltridecyl)chroman)acetic acid,2,5,7,8,-tetramethyl-(2R-(heptadecyl)chroman-6-yloxy) acetic acid, and 2,5,7,8,-tetramethyl-2R-(4,8,-dimethyl-1,3,7 E:Z nonotrien)chroman-6-yloxy) acetic acid.

16. The method of claim **14**, wherein said method is useful in the treatment of a cell proliferative disease.

* * * * *